Original paper

Autologous intradermal skin tests in women with Hashimoto's thyroiditis

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Abstract

Introduction: In a large proportion of patients with chronic urticaria, a coexisting autoimmune type of Hashimoto's thyroiditis is being diagnosed. An intradermal test with autologous serum has been generally considered as a screening procedure indicating the presence of triggering autoimmune inflammatory factors in the sera of patients with urticaria. These factors could be possibly involved in the pathogenesis of the disease. Now, it seems that in order to complete the screening diagnostic procedures of autoimmune component in patients with spontaneous chronic urticaria, intradermal tests with autologous plasma could be also useful.
Aim: To assess skin reactivity in patients suffering from the autoimmune type of Hashimoto's thyroiditis with serum and plasma intradermal tests.
Material and methods: Thirty-five female patients with Hashimoto's thyroiditis aged 23-78 years were recruited for our study. The control group consisted of 20 healthy volunteers with a negative history and no signs or symptoms of any thyroid as well as autoimmune diseases. Intradermal tests with autologous plasma, serum and with 0.9% NaCl (negative control) were performed.
Results: Five patients with the autoimmune type of Hashimoto's thyroiditis presented positive results of the autologous serum test (14.2%) while positive results of the autologous plasma test were obtained in 2 cases (5.7%). It seems to be important that subjects with positive results of intradermal tests have not been treated with L-thyroxine. In the case of healthy volunteers results of our diagnostic procedures were negative.
Conclusions: This study suggests that thyroid suppression by L-thyroxine can result in clinical remission of urticaria symptoms.

Key words: chronic urticaria, intradermal test, autoimmune thyroiditis.

Introduction

Urticaria is a common disease with highly complicated and not fully understood etiology. Pathogenesis of urticaria involves numerous inflammatory cells and their mediators released with or without involvement of various immunological mechanisms. Due to the diverse etiology, we distinguish several types and subtypes of urticaria. Often, despite a broad panel of diagnostic tests performed, specific causative factor or factors remain unknown. Therefore, in the case of up to 75% of patients with the chronic type of urticaria, an idiopathic variant is being diagnosed [1, 2]. In the group of chronic idiopathic urticaria (CIU), in 25-60% of cases the autoimmune origin (autoimmune urticaria – AIU) may be suspected [3, 4]. Moreover, in about 30% of patients suffering from chronic urticaria, autoimmune Hashimoto's thyroiditis is also diagnosed [5]. Autoimmune thyroiditis (Hashimoto's disease) is the most common type of inflammation of the thyroid gland. Although its etiopathogenesis is still unclear, it is defined as a polygenic disorder developing as a result of complex reactions between genetic and environmental factors. These factors lead to the breakdown of natural resistance to self-antigens and the development of auto-reactive lymphocytes and immunoglobulins [6].

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Association of AIU with Hashimoto's thyroiditis has not yet been elucidated. One of the first studies describing this relationship was published by Leznoff *et al.* in 1983 [7]. It has been reported by other authors that in 12-19% of patients with chronic urticaria, abnormalities in serum concentrations of thyroid hormones (fT3, fT4, TSH) are present. It is also known that thyroid auto-antibodies are not necessarily related to any specific dysfunction of the thyroid gland [8, 9].

The autologous serum skin test (ASST) is an intradermal test introduced as a screening procedure for the autoimmune type of chronic urticaria. The ASST was first described in 1986 by Grattan *et al*. [10] and since then, it has been widely used worldwide.

Aim

In 2009, the European Academy of Allergy and Clinical Immunology (EAACI) published guidelines for the use of ASST in the diagnosis of autoimmune urticaria [11]. There are also some new reports on the usefulness of the autologous plasma test (APST), which is another variant of screening intradermal diagnostic procedures, in the chronic type of the disease [12].

Material and methods

Thirty-five female patients with Hashimoto's thyroiditis aged 23-78 years (mean 46.4 years, median 47 years) were enrolled to the study. Hashimoto's thyroiditis was diagnosed on the basis of high serum levels of anti-TPO antibodies and/or anti-Tg antibodies and ultrasonographic criteria.

The average serum concentration of anti-Tg was 308 U/ml (normal range < 35 U/ml, median 75 ±542.8 U/ml), and anti-TPO – 1038 U/m (normal range < 35 U/m, median 675 ±1019.2 U/m).

All patients were euthyroid. Thirty out of 35 patients diagnosed with autoimmune Hashimoto's thyroiditis (85.7%) were treated with L-thyroxine with a dose of 25-125 μg. Detailed dermatological and autoimmunological evaluations of dermatological diseases have been performed. Any antihistaminic treatment has been taken at least 5 days before the diagnosis.

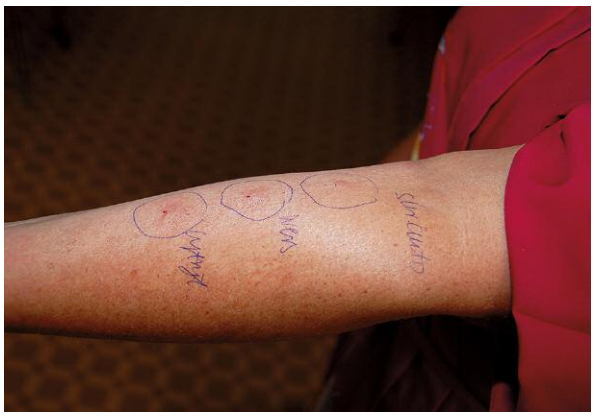

Fig. 1. Positive ASST and APST

The control group consisted of 20 healthy volunteers with a negative history and no signs or symptoms of any thyroid or autoimmune diseases.

The ASST has been performed according to the procedure proposed and described in EAACI guidelines. In the case of APST, two anticoagulants have been used and thereafter compared: sodium citrate and potassium edetate. 0.9% NaCl has been used as a negative control. Test results have been evaluated after 15 min and 30 min by two independent and well-trained physicians on the basis of the mean diameter of wheal and erythema. According to the EAACI guidelines and the Polish Allergological Society guidelines, a minimum difference of 1.5 mm in the mean perpendicular wheal diameter between the autologous serum-induced response and the saline-induced response should be used to define a positive response. Physiological saline (0.1 ml) was injected intradermally using the same method as for serum and plasma. The ASST and APST reading was conducted after 15 min and 30 min by two independent responsible workers. The mean diameter of erythema and wheal was measured.

Results

Five investigated patients have presented positive ASST results (14.2%), while a positive APST was obtained with sodium citrate as an anticoagulant in 2 patients (5.7%). In the case of all positive skin reactions, erythema and wheals, at least 3 mm diameter has been registered. They have remained for up to 60 min. Itching sensation at the injection site has been often reported by the patients. We have never observed any positive reaction neither to 0.9% NaCl nor in the control group of healthy volunteers.

Discussion

Pathogenesis of AIU still remains unclear, although it seems that IgG autoantibodies directed against α-fragment of high affinity IgE receptor (FcεRI) or IgE molecule might be involved. In addition, it seems that autoantibodies directed against thyroid antigens such as anti-TPO (against thyroid peroxidase) and anti-Tg (against thyroglobulin), which may induce the release of proinflammatory mediators are of certain importance [5].

There is increasing evidence that some cases of urticaria are associated with an ongoing autoimmune process in the thyroid gland. Thyroid autoimmunity occurs more frequently in patients with other skin diseases such as alopecia areata or vitiligo than in other immunologic diseases, which are rarely associated with skin eruptions in the nature of hives (type I diabetes) [13]. Anyhow, the influence of thyroid autoimmunity on the formation of skin lesions in urticaria is still unclear. Thyroid autoantibodies, generated due to inflammation are released into systemic

circulation, causing further stimulation of immune response. These antibodies might be considered to act as antigens, which cause agitation and degranulation of mast cells [14]. It has been also observed that anti-TPO antibodies may cross-react with peroxidase present in certain vegetables and therefore exacerbate the course of urticaria [15]. At present, there is growing evidence regarding the effects of thyroid hormone therapy in patients diagnosed with both urticaria and Hashimoto's thyroiditis, but these data are still contradictory [15, 16]. It seems that thyroid hormone therapy may be beneficial at least in some patients suffering from AIU. Efficacy of thyroxine in the treatment of patients with CIU has been evaluated by some researchers. Rumbyrt *et al.* also suggest that thyroid suppression can result in clinical remission of urticaria symptoms [16]. Our study may be concluded in a similar manner. The thyroid gland function should be investigated as one of important elements in the diagnosis of chronic urticaria. Even if physical examination does not indicate any ongoing pathological processes in the thyroid gland, this diagnostic approach should be followed [17].

It seems that thyroid autoimmunity may be an important factor in the pathogenesis of chronic urticaria and because of the therapy of AIU, further research on thyroid hormone therapy is absolutely necessary.

Conclusions

Chronic spontaneous urticaria is one of the most frequent skin disorders, and often people have been suffering from it for many years. It strongly affects the daily quality of life of patients. The AIU seems to be one of the most difficult to treat variants of CIU as the underlying cause of the disease still remains unclear. Autologous skin tests and evaluation of autoantibodies are recommended for the first-line diagnosis. High doses of non-sedating antihistamines are usually not effective and alternative therapeutical approaches including thyroid hormone therapy are necessary.

Usefulness of thyroid hormones in AIU therapy must be confirmed by additional studies and we look forward to seeing the results.

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